

**National Advisory Committee (NAC)
for Acute Exposure Guideline Levels (AEGLs) for Hazardous Substances**

September 16-17, 2003

Final Meeting-30 Highlights

U.S. Department of Labor
200 Constitution Avenue, N.W., Rm 4437-B,C,D
Washington, DC 20210

INTRODUCTION

The draft NAC/AEGL-29 meeting highlights were reviewed. There were no corrections or comments, and a motion was made by Loren Koller and seconded by John Hinz to accept the meeting highlights as presented. The motion passed unanimously by a voice vote. The final version of the NAC/AEGL-29 meeting highlights is attached (Appendix A) and was distributed to the NAC/AEGL by e-mail.

Ernie Falke discussed highlights of the July COT AEGL Subcommittee meeting. The COT subcommittee was concerned that the AEGL-2 and AEGL-3 values were very close for phosphine (less than a factor of 2), and questioned whether there should be a specific minimal difference between AEGL tiers because of the needs of emergency planners. It was pointed out that AEGL tiers for other chemicals, such as aniline, hydrogen cyanide and phosgene were also close together. George Rusch pointed out that in all of these cases the closeness of values reflects the exposure-response data (very steep concentration-response curve). After some discussion, the NAC felt that this closeness of values was appropriate and should be retained; doing otherwise would not reflect the toxicity of the chemical. Therefore, a comment will be added to the phosphine TSD acknowledging the closeness of the AEGL-2 and AEGL-3 values and explaining the basis of this closeness. Regarding the Level of Odor Awareness (LOA), the COT requested that the LOA methodology be published, either as an RIVM document or in the Journal of Inhalation Toxicology. Hopefully, this publication will precede the publication of any TSD that includes an LOA. The COT also requested that the following issues be addressed when the SOP is updated: RD_{50} and its use in developing AEGLs, benchmark dose approach, rounding and time-scaling, holding irritation concentrations stable across time, PBPK issues, modifying factor use, and time scaling vs. constant values for solvents (Attachment 1).

Ernie Falke distributed proposed chemical lists for NAC- 32, 33, 34, and 35 (March-December, 2004) and asked NAC members to volunteer to be chemical manager for these priority chemicals (Attachment 2).

A revised draft of language to be added to the SOP regarding use of occupational studies, prepared by John Morawetz, was reviewed. A motion was made by George Alexeeff and seconded by Richard Niemier to accept the revised language for inclusion into the SOP as presented. The motion passed unanimously by a voice vote (Attachment 3).

The highlights of the NAC/AEGL-30 meeting are summarized below along with the Meeting Agenda (Attachment 4) and the Attendee List (Attachment 5). The subject categories of the highlights do not necessarily follow the order listed in the NAC/AEGL-30 Agenda.

RESPONSES TO *FEDERAL REGISTER* COMMENTS ON THE PROPOSED AEGL VALUES

(A) Comments from the *Federal Register Notice* of July 18, 2003, on the proposed AEGL values for Phosphorus trichloride and Acetone cyanohydrin were received and discussed. The NAC/AEGL deliberation of these chemicals are briefly summarized as the following:

PHOSPHORUS TRICHLORIDE

Comments were received from John Morawetz regarding supporting data for AEGL-1. Human data from an abstract by Sassi (1952) were used as supporting information for AEGL-1 values. After discussion, it was agreed that it would be best to remove the Sassi report as support for AEGL-1 values due to ambiguities in the study report. A motion to move the chemical from proposed to interim status was made by John Morawetz and seconded by David Belluck. The motion was approved unanimously by the NAC/AEGL (Appendix B).

ACETONE CYANOHYDRIN

Comments were received from John Morawetz and the Methacrylate Producers Association, Inc. Mr. Morawetz was concerned that descriptions of two occupational hydrogen cyanide studies (El Ghawabi et al., 1975, and Leaser, 1990) were in need of revision. The descriptions of these studies will be made consistent with the study descriptions in the hydrogen cyanide TSD. Mark Hamilton made a presentation on behalf of the Methacrylate Producers Association, explaining that hydrogen cyanide (HCN) is the principal hazard from acetone cyanohydrin (ACN) exposure. The Association's comments stated that ACN volatilizes rapidly and almost completely to HCN and that ACN itself is not detected during a release. Therefore, no separate AEGL values are needed for ACN. If separate values for ACN are derived, the Methacrylate Producers Association stated that there would be no justification for setting ACN values lower than HCN values. Peter Griem then responded to the comments (Attachment 6). After discussion, a motion was made by Ernest Falke and seconded by Richard Thomas to adopt HCN AEGL-2 and AEGL-3 values as AEGL-2 and AEGL-3 values for ACN; and to remove the MF of 2 from the ACN AEGL-1 values; and to raise the document to interim status. The motion was approved unanimously by the NAC/AEGL (Appendix C). This approach used ACN data to

develop AEGL-1 values that are very similar to the HCN AEGL-1 values. A footnote will also be added stating that these are nominal values for ACH and actual exposure may include acetone, HCN, and ACN. The interim values are presented in the table below.

| Summary of Interim AEGL Values for Acetone Cyanohydrin [ppm] | | | | | | |
|---|------------|------------|--------|--------|--------|---|
| Classification | 10-minutes | 30-minutes | 1-hour | 4-hour | 8-hour | Endpoint (Reference) |
| AEGL-1 | 2.1 | 2.1 | 1.7 | 1.1 | 0.69 | Red nasal discharge in rats |
| AEGL-2 | 17 | 10 | 7.1 | 3.5 | 2.5 | HCN AEGL-2 values adopted as ACN AEGL-2 values |
| AEGL-3 | 27 | 21 | 15 | 8.6 | 6.6 | HCN AEGL-3 values adopted as ACN AEGL-3 values |

(B). No comments were received regarding the *Federal Register Notice* of May 28, 2003, on the proposed AEGL values for Fluorine, Jet Fuel, Monochloroacetic acid, and Phosphorus oxychloride. Therefore, these chemicals were elevated to Interim status as indicated below.

FLUORINE

No comments were received regarding the *Federal Register Notice* of July 18, 2003. A motion to move the chemical from proposed to interim status was made by Richard Niemier and seconded by Richard Thomas. The motion was approved unanimously by the NAC/AEGL (Appendix D).

JET FUEL

No comments were received regarding the *Federal Register Notices* of July 18, 2003. A motion to move the chemical from proposed to interim status was made by Richard Niemier and seconded by Richard Thomas. The motion was approved unanimously by the NAC/AEGL (Appendix E).

MONOCHLOROACETIC ACID

No comments were received regarding the *Federal Register Notices* of July 18, 2003. A motion to move the chemical from proposed to interim status was made by Richard Niemier and seconded by Richard Thomas. The motion was approved unanimously by the NAC/AEGL (Appendix F).

PHOSPHORUS OXYCHLORIDE

No comments were received regarding the *Federal Register Notices* of July 18, 2003. A motion to move the chemical from proposed to interim status was made by Richard Niemier and seconded by Richard Thomas. The motion was approved unanimously by the NAC/AEGL (Appendix G).

(C). Comments regarding the *Federal Register Notice* of July 18, 2003, on the proposed AEGL values for Bromine, Methyl ethyl ketone, Xylenes, and Ammonia were received and will be discussed at NAC-31 (December, 2003) due to the following reasons: Ammonia: The Fertilizer Institute requested, and received, a 60 day extension of the Public Comment Period; Bromine: extensive comments were very recently received; and Xylene and Methyl ethyl ketone are being evaluated to determine if PBPK modeling is feasible.

REVIEW AND RESOLUTION OF COT/AEGL COMMENTS

Phenol (CAS No. 108-95-2)

Chemical Manager: Robert Snyder
Staff Scientist: Peter Griem, FOBIG

Peter Griem discussed concerns expressed by the COT AEGL Subcommittee (Attachment 7). Major concerns were as follows: (1) All the AEGL values for phenol were too conservative and that the ERPG values were far more consistent with the phenol toxicologic profile; (2) Use of a NOAEL from a 2 week animal study as the basis of AEGL-1; (3) AEGL-2 values were derived as a fraction of the AEGL-3 values; and (4) Questionable validity of the AEGL-3 key study. After much discussion, a motion was made by George Rodgers and seconded by Richard Niemier to adopt revised AEGL-1 values of 8.3 ppm at all time points; AEGL-3 values of 200 ppm, 200 ppm, 160 ppm, 98 ppm, and 87 ppm for the 10-min, 30-min, 1-hr, 4-hr, and 8-hr time points, respectively; and AEGL-2 values of 1/3 the AEGL-3 values. (The rationale for this proposal is detailed in Attachment 7). The motion did not pass (YES:6: NO: 8; ABSTAIN: 2) (Appendix H). Further discussion of phenol was postponed until the December, 2003, meeting.

Carbon Monoxide (CAS No. 630-08-0)

Chemical Manager: George Rodgers
Staff Scientist: Peter Griem, FOBIG

Peter Griem discussed concerns expressed by the COT AEGL Subcommittee (Attachment 8). Major concerns were as follows: (1) AEGL-2 and AEGL-3 values for carbon monoxide were conservative; (2) Use of a 4% COHb as the basis of AEGL-2; and (3) Questionable validity of the

AEGL-3 key studies. After discussion, NAC consensus was not to change the proposed AEGL values for carbon monoxide. Rather, a cover letter will be written stating that communications with cardiologists indicated that they could not correlate signs/symptoms to the COHb level of concern (AEGL-2). The justification for AEGL-3 values will be strengthened, perhaps by using NAAQs (National Ambient Air Quality Standards) documentation as support. It was also requested that NAC members with supporting information send these data to Peter Griem.

Acrylic Acid (CAS No. 79-10-7)

Chemical Manager: Ernest Falke
Staff Scientist: Peter Griem, FOBIG

Dr. James McLaughlin, Chairman of the Basic Acrylic Monomer Manufacturers, Inc. (BAMM), provided additional data and a letter (Attachment 9) regarding the COT AEGL Subcommittee's comments on the acrylic acid TSD to assure that all information was considered. The letter had not been distributed to the NAC prior to the meeting. BAMMs major concerns were as follows: (1) An AEGL-1 value of 1.5 ppm is too low because RD_{50} work suggests the irritation threshold to be at or above 6-8 ppm. The Renshaw data supports an AEGL-1 of 5-10 ppm and is consistent with international consensus; (2) AEGL-3 values are substantially too low and cannot be reconciled with current data, especially nose-only vapor exposures; and (3) LOA values are subject to abuse unless it is clearly stated that no health effects are implied.

Peter Griem discussed concerns expressed by the COT AEGL Subcommittee (Attachment 10). The COT AEGL Subcommittee's major concerns were as follows: (1) Use of a personal communication as the key study for AEGL-1; (2) Use of histological changes of the olfactory epithelium as the basis of AEGL-2; and (3) Use of an aerosol study instead of a vapor study and use of the MLE_{01} instead of BMC_{05} as the basis of AEGL-3. After much discussion, the AEGL-1 values were increased from 1.0 ppm at all time points to 1.5 ppm at all time points. Rationale for this approach is presented on page 8 of Attachment 10. AEGL-2 and AEGL-3 values were retained.

REVIEW OF CHEMICAL WITH ISSUES FROM PREVIOUS MEETINGS

Vinyl Chloride (CAS No. 75-01-4)

Chemical Manager: Robert Benson
Staff Scientist: Fritz Kalberlah, FOBIG

Bob Benson, Chemical Manager, provided a brief update on the changes to the VC TSD. These changes included revision in the description of an occupational study, revision to the calculations

of cancer risk in the appendix, including an additional appendix describing additional assessment of cancer incidence from occupational exposure, and addition of a table with the cancer calculations to the Executive Summary. There have been no changes in the AEGL values previously approved by the Committee. As the cancer calculations do not require a formal vote of the committee, Bob proposed that the document (after editorial revisions) be submitted to the Federal Register and made available for public comment.

REVIEW of PRIORITY CHEMICALS

STYRENE (CAS No. 100-42-5)

Chemical Manager: Loren Koller
Staff Scientist: Jens-Uwe Voss, Toxicological consultant, Germany

Jens-Uwe Voss presented an overview of the database and AEGL development for styrene (Attachment 11). Ursula Gundert-Remy then presented information on sensitive populations. Various models have suggested that P450 activity in infants is > 5-fold less than in adults; therefore an intraspecies UF of 3 may not be sufficient for a newborn.

The proposed AEGL-1 value was based on a NOAEL for irritation in humans of 20 ppm (Seeber et al., 2002). The TSD scientist suggested applying an intraspecies uncertainty factor of 1, as the value is considered sufficiently conservative because only minor irritation and headache were noted at 50 ppm. A motion was made by George Rodgers and seconded by Richard Niemier to accept an AEGL-1 value of 20 ppm for all time points because there is adaptation to the slight irritation that defines the AEGL-1. The motion passed (YES: 14; NO: 1; ABSTAIN: 1) (Appendix I). It was noted that utilizing the minor irritation and headache noted at 50 ppm and applying an intraspecies UF of 3, yields a supporting value of 17 ppm.

The proposed AEGL-2 was based on CNS effects in humans during and after exposure to 376 ppm for 1 hour (Stewart et al., 1968). The TSD scientist suggested applying an intraspecies UF of 3 because toxicokinetic data for humans indicate several-fold higher blood levels at heavy exercise, but high exercise cannot be maintained for hours and the endpoint is considered below the level of CNS depression that could impair escape. Time scaling using $n=3$ was proposed for the 10- and 30-minute values, and the 4- and 8-hour AEGL-2 values were set equal to the 1-hour value because toxicokinetic data for humans indicate very little or no increase at exposure times greater than 1 hour. Ursula Gundert-Remy reminded the group that P450 activity data suggest that infants under 1 year of age may be 5-fold more susceptible due to lower P450 activity, and questioned if the UF of 3 was sufficient. Susan Ripple then summarized information from a continuous styrene release from a train car near an assisted living facility. Ten nurses and fifteen responders, exposed to a 1.5 hour TWA of 490 ppm (range 425 to 529 ppm 15 min breathing zone

samples), experienced headache, ocular and upper respiratory irritation, and nausea, while continuing work to evacuate residents. These data suggest that the proposed AEGL-2 values do not impair ability to escape. Susan will send this report to Paul Tobin. A motion was made by Bob Benson and seconded by Ernest Falke to accept the proposed AEGL-2 values of 230 ppm for 10-minutes, 160 ppm for 30-minutes, and 130 ppm for 1-, 4-, and 8-hours. The motion passed (YES: 13; NO: 3; ABSTAIN: 1) (Appendix I).

The proposed AEGL-3 was based on a 4-hour BMDL₀₅ of 3400 ppm in female rats (BASF, 1979). The TSD scientist suggested applying intraspecies and interspecies UFs of 3 each resulting in a total UF of 10. Time scaling using a chemical-specific, empirically derived n= 1.2 was proposed. Larry Gephart expressed concern over extrapolation from a 4-hour starting point to the 10-minute AEGL value. Concern was also expressed about extrapolation to 8-hours from the 4-hour starting point because toxicokinetic data for humans indicate very little or no increase at exposure times greater than 1 hour. A motion was made by Bob Snyder and seconded by Ernest Falke to accept the AEGL-3 values of 1900 ppm for 10- and 30-minutes, 1100 ppm for 1-hour, and 340 ppm 4-, and 8-hours. The motion passed (YES: 18; NO: 0; ABSTAIN: 0) (Appendix I).

The proposed LOA of 0.54 ppm was unanimously by a show of hands.

| Summary of AEGL Values for Styrene | | | | | | |
|------------------------------------|------------------------------------|------------------------------------|------------------------------------|-----------------------------------|-----------------------------------|---|
| Classification | 10-minute | 30-minute | 1-hour | 4-hour | 8-hour | Endpoint (Reference) |
| AEGL-1 | 20 ppm 85 mg/m ³ | 20 ppm 85 mg/m ³ | 20 ppm 85 mg/m ³ | 20 ppm 85 mg/m ³ | 20 ppm 85 mg/m ³ | NOAEL for irritation (Seeber et al., 2002) |
| AEGL-2 | 230 ppm 980 mg/m ³ | 160 ppm 680 mg/m ³ | 130 ppm 550 mg/m ³ | 130 ppm 550 mg/m ³ | 130 ppm 550 mg/m ³ | CNS effects - human (Stewart et al. 1968) |
| AEGL-3 | 1900 ppm 8090 mg/m ³ | 1900 ppm 8090 mg/m ³ | 1100 ppm 4690 mg/m ³ | 340 ppm 1450 mg/m ³ | 340 ppm 1450 mg/m ³ | BMDL ₀₅ in female rats (BASF, 1979) |

PROPANE CAS Reg. No.74-98-6

Chemical Manager: Larry Gephart
Staff Scientist: P. J. M. Bos, RIVM, The Netherlands

The chemical review on propane was presented by Peter Bos (Attachment 12). The proposed AEGL-1 values were based on no effects in humans exposed to 10,000 propane for 10 minutes (Patty and Yant, 1929). An intraspecies UF of 1 was proposed because of the very steep concentration-response curve (for butane) implying little interindividual variability. Time scaling using n= 3 was proposed for extrapolation to 30-minutes and 1-hour, and it was proposed that the 1-hour value be adopted as both the 4- and 8-hour AEGL-1 values because steady-state is reached within 30 minutes. Proposed AEGL-1 values for propane were 10,000 ppm for 10-min, 6900 ppm

for 30-min, and 5500 ppm for 1-, 4-, and 8-hours. It was noted that the AEGL-1 value is higher than 10% of the lower explosive limit of propane in air (LEL = 2.3% (23,000 ppm)). Therefore, safety considerations against hazard of explosion must be taken into account.

The proposed AEGL-2 values are based on a NOEL for cardiac sensitization in dogs at 50,000 ppm (Reinhardt et al., 1971). An intraspecies UF of 3 was proposed to protect sensitive individuals, and an interspecies UF of 1 was proposed because the dog is an optimized supersensitive model for humans. The value of 17,000 ppm was applied across all time points because cardiac sensitization is a concentration-related threshold effect. Because the AEGL-2 value is higher than 50% of the lower explosive limit of propane in air (LEL = 2.3% (23,000 ppm)), the AEGL-2 values were not presented in the Table, but rather in a footnote. Safety considerations against hazard of explosion must be taken into account.

The proposed AEGL-3 values are based on a concentration causing no deaths in a cardiac sensitization study in dogs at 100,000 ppm (Reinhardt et al., 1971). An intraspecies UF of 3 was proposed to protect sensitive individuals, and an interspecies UF of 1 was proposed because the dog is an optimized supersensitive model for humans. The value of 33,000 ppm was applied across all time points because cardiac sensitization is a concentration-related threshold effect. Because the AEGL-3 value is higher than 100% of the lower explosive limit of propane in air (LEL = 2.3% (23,000 ppm)), the AEGL-3 values were not presented in the Table, but rather in a footnote. Safety considerations against hazard of explosion must be taken into account.

After some discussion, a motion was made by Loren Koller and seconded by John Hinz to accept the AEGL-1, AEGL-2, and AEGL-3 values as proposed, changing the footnote for the AEGL-3 values to indicate that the values are >100% of the Lower Explosive Limit (LEL) (not above 50% of the LEL). The motion passed (YES: 17; NO: 1; ABSTAIN: 1) (Appendix J).

| Summary of AEGL Values for Propane | | | | | | |
|------------------------------------|---------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|---|
| Classification | 10-minute | 30-minute | 1-hour | 4-hour | 8-hour | Endpoint (Reference) |
| AEGL-1 | 10,000 ppm* 5550 mg/m ³ | 6900 ppm* 3830 mg/m ³ | 5500 ppm* 3050 mg/m ³ | 5500 ppm* 3050 mg/m ³ | 5500 ppm* 3050 mg/m ³ | NOEL in humans (Patty and Yant, 1929) |
| AEGL-2 | See below [†] | See below [†] | See below [†] | See below [†] | See below [†] | NOEL for cardiac sensitization in dogs (Reinhardt et al., 1971) |
| AEGL-3 | See below [‡] | See below [‡] | See below [‡] | See below [‡] | See below [‡] | No mortality in dogs (Reinhardt et al., 1971) |

*The AEGL-1 value is higher than 10% of the lower explosive limit of propane in air (LEL = 2.3% (23,000 ppm)). Therefore, safety considerations against hazard of explosion must be taken into account.

[†]The AEGL-2 value is higher than 50% of the lower explosive limit of propane in air (LEL = 2.3% (23,000 ppm)). Therefore, safety considerations against hazard of explosion must be taken into account. The calculated AEGL-2 values are held constant across all time periods: 17,000 ppm (9450 mg/m³).

*The AEGL-3 value is higher than 100% of the lower explosive limit of propane in air (LEL = 2.3% (23,000 ppm)). Therefore, safety considerations against hazard of explosion must be taken into account. The calculated AEGL-3 values are held constant across all time periods: 33,000 ppm (9450 mg/m³).

Butane
CAS No. 106-97-8

Chemical Manager: Larry Gephart
Staff Scientist: P. J. M. Bos, RIVM, The Netherlands

The chemical review on butane was presented by Peter Bos (Attachment 13). The proposed AEGL-1 values were based on no effects in humans exposed to 10,000 butane for 10 minutes (Patty and Yant, 1929). An intraspecies UF of 1 was proposed because of the very steep concentration-response curve implying little interindividual variability. Time scaling using $n=3$ was proposed for extrapolation to 30-minutes and 1-hour, and it was proposed that the 1-hour value be adopted as both the 4- and 8-hour AEGL-1 values because steady-state is reached within 30 minutes. Proposed AEGL-1 values for butane were 10,000 ppm for 10-min, 6900 ppm for 30-min, and 5500 ppm for 1-, 4-, and 8-hours. It was noted that, the AEGL-1 value is higher than 10% of the lower explosive limit of propane in air (LEL = 1.9% (19,000 ppm)). Therefore, safety considerations against hazard of explosion must be taken into account.

The proposed AEGL-2 values were based on a dazed appearance (but able to walk) in guinea pigs exposed to 50,000-56,000 ppm for 2 hours (Nuckolls, 1929). A total UF of 3 was proposed and considered sufficient because effects were due to butane and, thus, no large differences in kinetics would be expected and a higher UF would yield AEGL-2 values close to AEGL-1 values. Time scaling using $n=3$ was proposed for extrapolation to 10- and 30-minutes and 1-hour, and it was proposed that the 2-hour point of departure value be adopted as both the 4- and 8-hour AEGL-2 values because steady-state is reached within 30 minutes. Proposed AEGL-2 values for butane were 38,200 ppm for 10-min, 26,500 ppm for 30-min, 21,000 ppm for 1-hour, and 16,700 ppm for 4- and 8-hours. Because the AEGL-2 value is higher than 50% of the lower explosive limit of propane in air (LEL = 1.9% (19,000 ppm)), the AEGL-2 values were not presented in the Table, but rather in a footnote. Safety considerations against hazard of explosion must be taken into account.

The proposed AEGL-3 values were based on a calculated 2-hour LC_{01} in mice of 160,000 ppm (Shugaev, 1969). A total UF of 3 was proposed and considered sufficient because effects were due to butane and, thus, no large differences in kinetics would be expected, the steep concentration-response curve suggested small interindividual variability, and the most sensitive species was used. Time scaling using $n=3$ was proposed for extrapolation to 10- and 30-minutes and 1-hour, and it was proposed that the 2-hour point of departure value be adopted as both the 4- and 8-hour AEGL-2 values because steady-state is reached within 30 minutes. Proposed AEGL-3 values for butane were 122,000 ppm for 10-min, 85,000 ppm for 30-min, 67,000 ppm for 1-hour, and 53,000

ppm for 4-, and 8-hours. Because the AEGL-3 value is higher than 100% of the lower explosive limit of propane in air (LEL = 1.9% (19,000 ppm)), the AEGL-3 values were not presented in the Table, but rather in a footnote. Safety considerations against hazard of explosion must be taken into account.

After some discussion, a motion was made by John Hinz and seconded by George Rodgers to accept the AEGL-1 values as proposed, to accept AEGL-2 values of 25,000 ppm for 10-minutes and 17,000 ppm for 30-min, 1-, 4-, and 8-hours, and to accept AEGL-3 values of 76,000 ppm for 10-minutes and 53,000 ppm for 30-min, 1-, 4-, and 8-hours. The points of departure utilized for the AEGL-2 and AEGL-3 values are those described above. However, instead of scaling across time for the 30-min and 1-hr values, the 2-hr point of departures (with the UF of 3 applied) were held constant for the 30-min, 1-, 4-, and 8-hr time points, and time scaling using $n=3$ was applied to derive the 10-min AEGL-2 and AEGL-3 values because steady-state is reached within 30-minutes, but not within 10-minutes. The motion passed (YES: 17; NO: 1; ABSTAIN: 1) (Appendix K).

| Summary of AEGL Values for Butane | | | | | | |
|-----------------------------------|---------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|---|
| Classification | 10-minute | 30-minute | 1-hour | 4-hour | 8-hour | Endpoint (Reference) |
| AEGL-1 | 10,000 ppm* 4200 mg/m ³ | 6900 ppm* 2900 mg/m ³ | 5500 ppm* 2300 mg/m ³ | 5500 ppm* 2300 mg/m ³ | 5500 ppm* 2300 mg/m ³ | NOEL in humans (Patty and Yant, 1929) |
| AEGL-2 | See below [†] | See below [†] | See below [†] | See below [†] | See below [†] | dazed appearance (but able to walk) in guinea pigs (Nuckolls, 1929) |
| AEGL-3 | See below [‡] | See below [‡] | See below [‡] | See below [‡] | See below [‡] | calculated 2-hour LC ₀₁ in mice (Shugaev, 1969) |

*The AEGL-1 value is higher than 10% of the lower explosive limit of propane in air (LEL = 1.9% (19,000 ppm)). Therefore, safety considerations against hazard of explosion must be taken into account.

[†]The AEGL-2 value is higher than 50% of the lower explosive limit of propane in air (LEL = 1.9% (19,000 ppm)). Therefore, safety considerations against hazard of explosion must be taken into account. The calculated AEGL-2 values are: 25,000 ppm (11,000 mg/m³) for 10-min, and 17,000 ppm (7000 mg/m³) for 30-min, and 1-, 4-, and 8-hours.

[‡]The AEGL-3 value is higher than 100% of the lower explosive limit of propane in air (LEL = 1.9% (19,000 ppm)). Therefore, safety considerations against hazard of explosion must be taken into account. The calculated AEGL-3 values are 76,000 ppm for 10-min, and 53,000 ppm (23,000 mg/m³) for 30-min, and 1-, 4-, and 8-hours.

Dimethylsulfate
CAS No. 77-78-1

Staff Scientist: Susanne Gfatter, FOBIG
Chemical Manager: Bob Snyder

Susanne Gfatter described the data base for dimethylsulfate (Attachment 14). The proposed AEGL-1 was based on a 14-day repeated exposure study in rats (Frame et al. 1993; abstract publication). At 0.1 ppm for 6-hour, altered nasal cell proliferation without histopathological findings was observed. Evidence of only modest differences in toxicokinetics and toxicodynamics is available, therefore an interspecies factor of 3 is applied. The interspecies factor was further justified because the critical study used repeated exposure (Frame et al. 1993). No large differences in susceptibility between individuals are expected for nonspecific irritating effects, therefore an intraspecies factor of 3 is chosen. Default time scaling exponents of $n=1$ for extrapolation to 8-hr and $n=3$ when extrapolating to 30-min, 1-hr and 4-hr were proposed; the 10-min AEGL-1 was set equal to the 30-min value. Proposed AEGL-1 values were 0.023 ppm for 10- and 30-min, 0.018 ppm for 1-hour, 0.011 ppm for 4-hr, and 0.0075 ppm for 8-hr.

The proposed AEGL-2 values were based on asthma-like breathing sounds in rats, mice, and golden hamsters at exposed to 0.5 ppm for 6-hours (Schlögel, 1972). Evidence of only modest differences in toxicokinetics and toxicodynamics is available, therefore an interspecies factor of 3 was proposed. No large differences in susceptibility between individuals are expected for nonspecific irritating effects, therefore an intraspecies factor of 3 was proposed. Default time scaling exponents of $n=1$ for extrapolation to 8-hr and $n=3$ when extrapolating to 30-min, 1-hr and 4-hr were proposed; the 10-min AEGL-2 was set equal to the 30-min value. Proposed AEGL-2 values were 0.11 ppm for 10- and 30-min, 0.091 ppm for 1-hour, 0.057 ppm for 4-hr, and 0.038 ppm for 8-hr.

The proposed AEGL-3 values were based a calculated 1-hr $BMCL_{05}$ of 5.8 ppm in guinea pigs (Hein, 1969). Evidence of only modest differences in toxicokinetics and toxicodynamics is available, therefore an interspecies factor of 3 was proposed. No large differences in susceptibility between individuals are expected for nonspecific irritating effects, therefore an intraspecies factor of 3 was proposed. Default time scaling exponents of $n=1$ for extrapolation to 4- and 8-hr and $n=3$ when extrapolating to 10- and 30-min were proposed. Proposed AEGL-3 values were 1.1 ppm for 10-min, 0.73 ppm for 30-min, 0.58 ppm for 1-hour, 0.15 ppm for 4-hr, and 0.073 ppm for 8-hr.

Discussion included the selection of the exponent, n , for scaling across time. LC_{50} values derived in rats of 64 ppm for an 1-hour duration (Hein, 1969) and of 32 ppm for a 4-hour exposure (Kennedy and Graepel, 1991) support the equation $C^2 \times t = k$. A similar time relationship was observed within mice, for which LC_{50} values of 98 ppm and 54 ppm were reported for an 1-hour and a 4-hour exposure, respectively (Hein, 1969; Molodkina et al. 1986). Discussion also involved selection of the key study for AEGL-3 derivation; it was suggested that the highest non-lethal concentration of 49 ppm (rats, 1-h exposure) be used for the derivation of the AEGL-3 values.

A motion was made by Loren Koller and Seconded by Ernest Falke to adopt AEGL-1 values of 0.035 ppm for 10- and 30-min, 0.024 ppm for 1-hr, 0.012 ppm for 4-hr and 0.0087 ppm for 8-hr; AEGL-2 values of 0.17 ppm for 10- and 30-min, 0.12 ppm for 1-hr, 0.061 ppm for 4-hr and 0.043 ppm for 8-hr; and AEGL-3 values of 12 ppm for 10-min, 6.9 ppm for 30-min, 4.9 ppm for 1-hr, 2.5 ppm for 4-hr and 1.7 ppm for 8-hr. These AEGL-1 and AGEL-2 values were based on the key

studies/point of departure and UFs described in the proposals above; however, time scaling used $n=2$. These AEGL-3 values were based on the highest concentration causing no deaths in rats (49 ppm, 1 hr), a total UF of 10, and time scaling using $n = 2$. The three AEGL tiers were balloted separately. The motion passed for AEGL-1 and AEGL-2 (YES: 19; NO: 0; ABSTAIN: 1) (Appendix L). The motion did not pass for AEGL-3 (YES: 6; NO: 8; ABSTAIN: 1) (Appendix L).

A motion was then made by Richard Thomas and seconded by Richard Niemier to adopt AEGL-3 values of 4.0 ppm for 10- min, 2.3 ppm for 30-min, 1.8 ppm for 1-hr, 0.82 ppm for 4-hr and 0.58 ppm for 8-hr. These AEGL-3 values were based on the highest concentration causing no deaths in rats (49 ppm for 1hr), a total UF of 30 (intra =3, inter =10 because the rat is not the most sensitive species), and time scaling using $n = 2$. The motion passed (YES: 19; NO: 0; ABSTAIN: 1) (Appendix L).

| Summary of AEGL Values for Dimethylsulfate | | | | | | |
|--|-------------------------------------|------------------------------------|-------------------------------------|--------------------------------------|---------------------------------------|---|
| Classification | 10-minute | 30-minute | 1-hour | 4-hour | 8-hour | Endpoint (Reference) |
| AEGL-1 | 0.035 ppm 0.18 mg/m ³ | 0.035 ppm 0.18mg/m ³ | 0.024 ppm 0.12 mg/m ³ | 0.012 ppm 0.062 mg/m ³ | 0.0087 ppm 0.045 mg/m ³ | nasal cell proliferation in rat (Frame et al., 1993) |
| AEGL-2 | 0.17 ppm 0.88 mg/m ³ | 0.17 ppm 0.88 mg/m ³ | 0.12 ppm 0.62 mg/m ³ | 0.061 ppm 0.32 mg/m ³ | 0.043 ppm 0.22 mg/m ³ | breathing problems rat, mouse, hamster (Schlogel, 1972) |
| AEGL-3 | 4.0 ppm 21 mg/m ³ | 2.3 ppm 12 mg/m ³ | 1.6 ppm 8.3 mg/m ³ | 0.82 ppm 4.3 mg/m ³ | 0.58 ppm 3.0 mg/m ³ | Concentration causing no death in rats (Hein, 1969) |

ALIPHATIC NITRILES

Acetonitrile (CAS No. 75-05-8)
 Isobutyronitrile (CAS No. 78-82-0)
 Propionitrile (Cas No. 107-12-0)
 Chloroacetonitrile (Cas No. 107-14-2)
 Malononitrile (Cas No. 109-77-3)

Staff Scientist: Cheryl Bast, ORNL
Chemical Manager: George Rodgers

Cheryl Bast presented an overview of the five nitrile compounds addressed in the TSD (Attachment 15). The aliphatic nitriles metabolically liberate cyanide via cytochrome P450

mediated hydroxylation on the carbon alpha to the cyano group and the toxicity of these nitriles is due to cyanide. The relative toxicity of the nitriles is due to the rate of cyanide liberation; generally, the nitriles that are metabolized most quickly or easily at the carbon atom alpha to the cyano group (α -carbon) are more toxic than nitriles metabolized more slowly at the α -carbon.

Acetonitrile (CAS No. 75-05-8)

The proposed AEGL-1 was based on slight chest tightness and cooling sensation in the lungs noted by one of three human male volunteers exposed to 40 ppm acetonitrile for 4 hours (Pozzani et al., 1959). No intraspecies uncertainty factor was applied because the mild effects are considered to have occurred in a sensitive subject since no symptoms were reported by two other subjects exposed to this same regimen and no effects were noted at 80 ppm for 4 hours by these same two subjects. The 40 ppm concentration was held constant across all time points because no human data exist for periods of less than 4-hours; thus, time-scaling to shorter durations could yield values eliciting symptoms above those defined by AEGL-1.

The proposed AEGL-2 was based on slight pulmonary congestion or hemorrhage in rats exposed to 4000 ppm acetonitrile for 4 hours (Pozzani et al., 1959). An uncertainty factor of 10 was used to extrapolate from animals to humans because the rat is not the most sensitive species. An uncertainty factor of 3 was applied to account for sensitive individuals because human accidental and occupational exposures indicate that there are individual differences in sensitivity to HCN but the magnitude of these differences does not appear to be great and AEGL-2 values derived with a total default uncertainty factor would yield values inconsistent with available human data. For scaling the AEGL-2 values for acetonitrile across time, the empirically-derived chemical-specific value of 2.5 (derived from rat lethality data ranging from 15 minutes to 8 hours exposure duration), was used as the exponent, n . The 30-minute AEGL-2 was also adopted as the 10-minute value due to the added uncertainty of extrapolating from a 4-hour time point to 10-minutes. Proposed AEGL-2 values were 310 ppm for 10- and 30-min, 230 ppm for 1 hour, 130 ppm for 4 hours, and 100 ppm for 8-hours.

The proposed AEGL-3 was based on a calculated 4-hour rat LC_{01} of 8421 ppm (Monsanto, 1986). An uncertainty factor of 10 was used to extrapolate from animals to humans because the rat is not the most sensitive species. An uncertainty factor of 3 was applied to account for sensitive individuals because human accidental and occupational exposures indicate that there are individual differences in sensitivity to HCN but the magnitude of these differences does not appear to be great, and AEGL-3 values derived with a total default uncertainty factor would be inconsistent with the total database (For scaling the AEGL values for acetonitrile across time, the empirically-derived chemical-specific value of 2.5 (derived from rat lethality data ranging from 15 minutes to 8 hours exposure duration), was used as the exponent, n . The 30-minute AEGL-3 was also adopted as the 10-minute value due to the added uncertainty of extrapolating from a 4-hour time point to 10-minutes. Proposed AEGL-3 values were 650 ppm for 10- and 30-min, 490 ppm for 1 hour, 280 ppm for 4 hours, and 210 ppm for 8-hours.

A motion was made by George Rodgers and seconded by John Hinz to accept the AEGL-values as presented. The AEGL-1, -2, and -3 values were polled separately. The motion did not pass for AEGL-1 (YES: 7; NO: 10; ABSTAIN: 1) (Appendix M). The motion passed for AEGL-2 (YES: 16; NO: 2; ABSTAIN: 2) (Appendix M), and AEGL-3 (YES: 17; NO: 2; ABSTAIN: 1) (Appendix M).

Concern was expressed about the sparse data set for AEGL-1. A motion was made by Bob Benson and seconded by John Morawetz to apply a modifying factor of 3 to the proposed AEGL-1 values to account for the sparse data set, yielding an AEGL-1 value of 13 ppm for all time points. The motion passed (YES: 19; NO: 1; ABSTAIN: 0) (Appendix M).

| Summary of AEGL Values For Acetonitrile | | | | | | |
|---|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|--|
| Classification | 10-Minute | 30-Minute | 1-Hour | 4-Hour | 8-Hour | Endpoint (Reference) |
| AEGL-1 | 13 ppm 22 mg/m ³ | 13 ppm 22 mg/m ³ | 13 ppm 22 mg/m ³ | 13 ppm 22 mg/m ³ | 13 ppm 22 mg/m ³ | Slight chest tightness and cooling sensation in lung (1/3 human volunteers) (Pozzani et al., 1959) |
| AEGL-2 | 310 ppm (520 mg/m ³) | 310 ppm (520 mg/m ³) | 230 ppm (390 mg/m ³) | 130 ppm (218 mg/m ³) | 100 ppm (168 mg/m ³) | Slight pulmonary congestion and hemorrhage in rats (Pozzani et al., 1959) |
| AEGL-3 | 650 ppm 1092 mg/m ³ | 650 ppm 1092 mg/m ³ | 490 ppm 820 mg/m ³ | 280 ppm 470 mg/m ³ | 213 ppm 360 mg/m ³ | Calculated LC ₀₁ in the rat after a 4-hour exposure (Monsanto, 1986) |

Isobutyronitrile (CAS No. 78-82-0)

Data were insufficient for derivation of AEGL-1 values for isobutyronitrile. The proposed AEGL-2 was based on a no-effect-level for maternal and fetal toxicity from a developmental toxicity study in rats (100 ppm, 6 hour/day, days 6-20 of gestation) (Saillenfait et al., 1993). An uncertainty factor of 3 was applied to account for sensitive individuals because human accidental and occupational exposures indicate that there are individual differences in sensitivity to HCN, but the magnitude of these differences does not appear to be great. An interspecies uncertainty factor of 3 was also applied because use of the full uncertainty factor of 10, would yield AEGL-2 values that are not consistent with the total data set. An *n* of 3 was applied to extrapolate to the 10-minute, 30-minute, 1-hour, and 4-hour time periods, and an *n* of 1 was applied to extrapolate to the 8-hour time period, to provide AEGL values that would be protective of human health. Proposed AEGL-2 values were 33 ppm for 10-min, 23 ppm for 30-min, 18 ppm for 1 hour, 11 ppm for 4 hours, and 7.5 ppm for 8-hours.

The proposed AEGL-3 was based on a calculated 1-hour LC_{01} of 677 ppm in rats (Eastman Kodak Co., 1986a). An uncertainty factor of 3 was applied to account for sensitive individuals because human accidental and occupational exposures indicate that there are individual differences in sensitivity to HCN, but the magnitude of these differences does not appear to be great. An interspecies uncertainty factor of 3 was also applied because use of the full uncertainty factor of 10, would yield AEGL-3 values that are not consistent with the total data set. An n of 3 was applied to extrapolate to the 10- and 30-minute time periods, and an n of 1 was applied to extrapolate to the 4- and 8-hour time periods. were 120 ppm for 10-min, 85 ppm for 30-min, 68 ppm for 1 hour, 17 ppm for 4 hours, and 8.5 ppm for 8-hours.

After discussion, a motion was made by Ernest Falke and seconded by John Hinz to accept the AEGL-2, and -3 values as presented and "NR" for AEGL-1. The motion passed (YES: 15; NO: 3; ABSTAIN: 0) (Appendix N), and AEGL-3 (YES: 17; NO: 2; ABSTAIN: 1).

| Summary of AEGL Values for Isobutyronitrile | | | | | | |
|---|----------------------------------|---------------------------------|--------------------------------|--------------------------------|---------------------------------|--|
| Classification | 10-minute | 30-minute | 1-hour | 4-hour | 8-hour | Endpoint (Reference) |
| AEGL-1 | NR* | NR | NR | NR | NR | Insufficient data to derive AEGL-1 values |
| AEGL-2 | 33 ppm 93 mg/m ³ | 23 ppm 65 mg/m ³ | 18 ppm 51 mg/m ³ | 11 ppm 31 mg/m ³ | 7.5 ppm 21 mg/m ³ | No-effect-level in rats (Saillenfait et al., 1993) |
| AEGL-3 | 123 ppm 350 mg/m ³ | 85 ppm 240 mg/m ³ | 68 ppm 190mg/m ³ | 17 ppm 48 mg/m ³ | 8.5 ppm 24 mg/m ³ | Calculated 1-hr LC_{01} in rats (Eastman Kodak, 1986a) |

NR: Not Recommended.

Propionitrile (Cas No. 107-12-0)

Chemical-specific data are insufficient for the derivation of AEGL-1 values for propionitrile. Appropriate i.p. toxicity data are available for both acetonitrile and propionitrile; thus, it was proposed to derive AEGL-1 values for propionitrile by analogy to acetonitrile AEGL-1 values. Mouse i.p. LD_{50} data suggest that propionitrile is approximately 21 times more toxic than acetonitrile. Therefore, the acetonitrile AEGL-1 values were divided by 21 to approximate AEGL-1 values for propionitrile. A modifying factor of 2 was also applied because the data suggesting that propionitrile is 21 times more toxic than acetonitrile are very limited, and thus, the value cannot be predicted with great precision. The proposed AEGL-1 value was 4.3 ppm at all time points.

The proposed AEGL-2 was based on headache, nausea, dizziness, vomiting, confusion, and disorientation in a 34-year-old male worker exposed to approximately 34 ppm propionitrile for 2 hours (Scolnick et al., 1993). An uncertainty factor of 3 was applied to account for sensitive individuals because human accidental and occupational exposures indicate that there are individual

differences in sensitivity to HCN but the magnitude of these differences does not appear to be great. An *n* of 3 was applied to extrapolate to the 30-minute and 1-hour time periods, and an *n* of 1 was applied to extrapolate to the 4- and 8-hour time periods. The 30-minute AEGL-2 value was also adopted as the 10-minute value due to the fact that reliable data are limited to durations ≥ 2 hours, and it is considered inappropriate to extrapolate back to 10-minutes. Proposed AEGL-2 values were 18 ppm for 10- and 30-min, 14 ppm for 1 hour, 5.7 ppm for 4 hours, and 2.8 ppm for 8-hours.

The proposed AEGL-3 was based on the highest concentration (690 ppm) causing no mortality in rats exposed to propionitrile for four hours (Younger Labs, 1978). An interspecies uncertainty factor of 10 was applied because the rat is not the most sensitive species. An uncertainty factor of 3 was applied to account for sensitive individuals. An *n* of 3 was applied to extrapolate to the 30-minute and 1-hour time periods, and an *n* of 1 was applied to extrapolate to the 8-hour time period. The 30-minute AEGL-3 value was also adopted as the 10-minute value due to the fact that the values are derived from a 4 hour exposure, and it is considered inappropriate to extrapolate back to 10-minutes. Proposed AEGL-3 values were 46 ppm for 10- and 30-min, 37 ppm for 1 hour, 23 ppm for 4 hours, and 12 ppm for 8-hours.

Discussion centered around the appropriateness of deriving AEGL-1 values for propionitrile by analogy to acetonitrile utilizing i.p. data. The NAC felt that this approach may be valid for effects defined by AEGL-2 or AEGL-3, but not effects defined by AEGL-1. Concern was also expressed that the data set for AEGL-2 is limited (the human accidental exposure included only 2 workers) and that perhaps a modifying factor for a sparse data base is appropriate. Ursula Gundert-Remy expressed concern that the proposed AEGL-3 values were very close to the human accidental exposure of 34 ppm for 7 hours that would have likely resulted in death had medical intervention not been obtained.

A motion was made by John Morawetz and seconded by Bob Benson to not recommend AEGL-1 values for propionitrile and to apply a modifying factor of 2 to the proposed AEGL-2 values to account for the sparse data set, yielding AEGL-2 values of 9.0 ppm for 10- and 30-min, 7.0 ppm for 1-hr, 2.9 ppm for 4-hr, and 1.4 ppm. The AEGL-1 motion passed (YES: 17; NO: 0; ABSTAIN: 0) (Appendix O). The AEGL-2 motion passed (YES: 16; NO: 1; ABSTAIN: 0) (Appendix O). A motion was then made by Bob Benson and seconded by George Rodgers to accept AEGL-3 values as proposed. The AEGL-3 motion passed (YES: 17; NO: 0; ABSTAIN: 0) (Appendix O).

| Summary of AEGL Values for Propionitrile | | | | | | |
|--|---------------------------------|---------------------------------|---------------------------------|----------------------------------|----------------------------------|---|
| Classification | 10-minute | 30-minute | 1-hour | 4-hour | 8-hour | Endpoint (Reference) |
| AEGL-1 (Nondisabling) | NR | NR | NR | NR | NR | |
| AEGL-2 (Disabling) | 9.0 ppm 20 mg/m ³ | 9.0 ppm 20 mg/m ³ | 7.0 ppm 16 mg/m ³ | 2.9 ppm 6.5 mg/m ³ | 1.4 ppm 3.2 mg/m ³ | Headache, nausea, vomiting, dizziness, confusion in a human subject (Scolnick et al., 1993) |

| | | | | | | |
|--------------------|---------------------------------|---------------------------------|--------------------------------|--------------------------------|-------------------------------|---|
| AEGL-3 (Lethal) | 46 ppm 100 mg/m ³ | 46 ppm 100 mg/m ³ | 37 ppm 83 mg/m ³ | 23 ppm 52 mg/m ³ | 12 ppm 7 mg/m ³ | Highest concentration causing no death in rats (Younger Labs, 1978) |
|--------------------|---------------------------------|---------------------------------|--------------------------------|--------------------------------|-------------------------------|---|

NR: Not Recommended

Chloroacetonitrile (Cas No. 107-14-2)

Chemical-specific data were insufficient for the derivation of AEGL-1, AEGL-2, or AEGL-3 values for chloroacetonitrile. In the absence of relevant chemical-specific data for chloroacetonitrile, it was proposed that a modification of the AEGL values for acetonitrile be utilized to derive AEGL-values for chloroacetonitrile. Mouse i.p. LD₅₀ data suggest that chloroacetonitrile is approximately 5.2 times more toxic than acetonitrile. Therefore, the acetonitrile values were divided by 5.2 to approximate AEGL values for chloroacetonitrile. In the absence of inhalation data, the i.p. route was considered the most appropriate for approximating inhalation toxicity values because both routes involve entry into the organism through a semipermeable membrane (peritoneal membrane and alveolar membrane) before diffusion into the blood. Furthermore, the magnitude and rate of effect (in descending order) for the different routes of administration are: intravenous, inhalation, intra peritoneal, subcutaneous, intramuscular, intradermal, oral, and topical (Klaassen, 1986).

During discussion, it was pointed out that molar equivalents must be used (not mg/kg comparisons) when determining relative toxicities from i.p. lethality data. On a molar basis, chloroacetonitrile is approximately 10 times more toxic than acetonitrile. A motion was made by Bob Benson and seconded by Richard Niemier to not recommend AEGL-1 values, to divide the acetonitrile AEGL-2 values by 2 to obtain AEGL-2 values for chloroacetonitrile (31 ppm for 10- and 30-min, 23 ppm for 1-hr, 13 ppm for 4-hr, and 10 ppm for 8-hr ppm), and to divide the acetonitrile AEGL-3 values by 10 to obtain AEGL-3 values for chloroacetonitrile (65 ppm for 10- and 30-min, 49 ppm for 1-hr, 28 ppm for 4-hr, and 21 ppm for 8-hr ppm). The motion passed (YES: 12; NO: 1; ABSTAIN: 3) (Appendix P).

| Summary of AEGL Values for Chloroacetonitrile | | | | | | |
|---|---------------------------------|---------------------------------|--------------------------------|--------------------------------|--------------------------------|---|
| Classification | 10-minute | 30-minute | 1-hour | 4-hour | 8-hour | Endpoint (Reference) |
| AEGL-1 | NR | NR | NR | NR | NR | |
| AEGL-2 | 31 ppm 52 mg/m ³ | 31 ppm 52 mg/m ³ | 23 ppm 39mg/m ³ | 13 ppm 22 mg/m ³ | 10 ppm 17 mg/m ³ | Derived by analogy to acetonitrile AEGL-2 values |
| AEGL-3 | 65 ppm 110 mg/m ³ | 65 ppm 110 mg/m ³ | 49 ppm 82 mg/m ³ | 28 ppm 47 mg/m ³ | 21 ppm 36 mg/m ³ | Derived by analogy to acetonitrile AEGL-3 values |

NR: Not Recommended

Malononitrile (Cas No. 109-77-3)

Chemical-specific data were insufficient for the derivation of AEGL-1, AEGL-2, or AEGL-3 values for malononitrile. In the absence of relevant chemical-specific data for malononitrile, it was proposed that a modification of the AEGL values for acetonitrile be utilized to derive AEGL-values for chloroacetonitrile. Mouse i.p. LD₅₀ data suggest that chloroacetonitrile is approximately 65 times more toxic than acetonitrile on a molar basis.

A motion was made by Bob Benson and seconded by Ernest Falke to not recommend AEGL-1 values, to divide the acetonitrile AEGL-2 values by 65 to obtain AEGL-2 values for malononitrile (4.8 ppm for 10- and 30-min, 3.5 ppm for 1-hr, 2.0 ppm for 4-hr, and 1.5 ppm for 8-hr ppm), and to divide the acetonitrile AEGL-3 values by 65 to obtain AEGL-3 values for malononitrile (10 ppm for 10- and 30-min, 7.5 ppm for 1-hr, 4.3 ppm for 4-hr, and 3.2 ppm for 8-hr ppm). The motion passed (YES: 15; NO: 0; ABSTAIN: 0) (Appendix Q).

| Summary of AEGL Values for Malononitrile | | | | | | |
|--|----------------------------------|----------------------------------|----------------------------------|----------------------------------|----------------------------------|---|
| Classification | 10-minute | 30-minute | 1-hour | 4-hour | 8-hour | Endpoint (Reference) |
| AEGL-1 (Nondisabling) | NR | NR | NR | NR | NR | |
| AEGL-2 (Disabling) | 4.8 ppm 8.0 mg/m ³ | 4.8 ppm 8.0 mg/m ³ | 3.5 ppm 6.0 mg/m ³ | 2.0 ppm 3.4 mg/m ³ | 1.5 ppm 2.6 mg/m ³ | Derived by analogy to acetonitrile AEGL-2 values |
| AEGL-3 (Lethal) | 10 ppm 17 mg/m ³ | 10 ppm 17 mg/m ³ | 7.5 ppm 13 mg/m ³ | 4.3 ppm 7.2 mg/m ³ | 3.2 ppm 5.5 mg/m ³ | Derived by analogy to acetonitrile AEGL-3 values |

Administrative Matters

The site and time of the next meeting, NAC/AEGL-31, will be December 10-12, 2003 in San Antonio, Texas.

All items in the agenda were discussed as thoroughly as the time permitted. The meeting highlights were prepared by Cheryl Bast and Robert Young, Oak Ridge National Laboratory, with input from the respective chemical managers, authors, and other contributors.

LIST OF ATTACHMENTS

The attachments were distributed during the meeting and will be filed in the EPA Docket Office.

- Attachment 1. Highlights of the COT/AEGL Subcommittee Meeting
- Attachment 2. List of chemicals to be considered at the NAC-32, 33, 34, and 35
- Attachment 3. Proposal for Evaluation of Occupational Monitoring Studies for inclusion in the SOP
- Attachment 4. NAC/AEGL-30 Meeting Agenda
- Attachment 5. NAC/AEGL-30 Attendee List
- Attachment 6. Response to Federal Register comments for acetone cyanohydrin
- Attachment 7. Response to COT subcommittee comments for phenol
- Attachment 8. Response to COT subcommittee comments for carbon monoxide
- Attachment 9. BMM comments on acrylic acid
- Attachment 10. Response to COT subcommittee comments for acrylic acid
- Attachment 11. Data Analysis of styrene
- Attachment 12. Data Analysis of propane
- Attachment 13. Data Analysis of butane
- Attachment 14. Data Analysis of dimethyl sulfate
- Attachment 15. Data Analysis of aliphatic nitriles

LIST OF APPENDICES

- Appendix A. Revised meeting highlights of NAC/AEGL-29
- Appendix B. Ballot for phosphorus trichloride
- Appendix C. Ballot for acetone cyanohydrin
- Appendix D. Ballot for fluorine
- Appendix E. Ballot for jet fuel
- Appendix F. Ballot for monochloroacetic acid
- Appendix G. Ballot for phosphorus oxychloride
- Appendix H. Ballot for phenol
- Appendix I. Ballot for styrene
- Appendix J. Ballot for propane
- Appendix K. Ballot for butane
- Appendix L. Ballot for dimethyl sulfate
- Appendix M. Ballot for acetonitrile
- Appendix N. Ballot for isobutyronitrile
- Appendix O. Ballot for propionitrile
- Appendix P. Ballot for chloroacetonitrile
- Appendix Q. Ballot for malononitrile